

WE CLAIM:

1. A method for amplifying a first nucleotide sequence and a second nucleotide sequence which are complementary and together form a double stranded DNA molecule, said method comprising:
  - 5 providing a sample containing the first and second nucleotide sequences;
  - providing a first oligonucleotide set of at least two oligonucleotides suitable for ligation together at a first ligation junction and for  
10 hybridization without mismatch to the first nucleotide sequence, wherein the at least two oligonucleotides hybridize on the first nucleotide sequence;
  - providing a second oligonucleotide set of at least two oligonucleotides suitable for ligation together at a second ligation junction and for hybridization without mismatch to the second nucleotide sequence, wherein the at  
15 least two oligonucleotides of the second oligonucleotide set hybridize on the second nucleotide sequence;
  - providing a ligase;
  - blending the sample, the first oligonucleotide set, the second oligonucleotide set, and the ligase to form an amplification mixture; and  
20 subjecting the amplification mixture to a series of cycles comprising a denaturation treatment and a thermal hybridization to amplify exponentially the first and second nucleotide sequences, wherein the at least two oligonucleotides of the second oligonucleotide set are complementary to the first oligonucleotide set with an oligonucleotide from the first oligonucleotide set  
25 complementing an oligonucleotide from the second oligonucleotide set with a single base overhang.
2. The method according to claim 1, wherein the ligase is a thermostable ligase which does not become irreversibly denatured and lose its  
30 catalytic activity when subjected to temperatures ranging from about 50° C. to 105° C.

3. A method for together amplifying nucleotide sequences which are complementary and together form double stranded DNA molecules with one double-stranded DNA molecule having a genetic defect and another double-stranded DNA molecule having a normal form of the complementary nucleotide sequence, said method comprising:
- 5 providing a sample potentially containing a double-stranded DNA molecule with a nucleotide sequence having a genetic defect and a double-stranded DNA molecule with a normal form of the nucleotide sequence;
- providing a first oligonucleotide set of at least two
- 10 oligonucleotides suitable for ligation together at a first ligation junction and for hybridization without mismatch to the nucleotide sequence with the genetic defect, but not to the nucleotide sequence with the normal form, wherein the oligonucleotides of the first set hybridize on the nucleotide sequence with the genetic defect;
- 15 providing a second oligonucleotide set of at least two oligonucleotides suitable for ligation together at a second ligation junction and for hybridization without mismatch to the nucleotide sequence with the normal form, but not to the nucleotide sequence with the genetic defect, wherein the oligonucleotides of the second set hybridize on the nucleotide sequence with the
- 20 normal form;
- providing a third oligonucleotide set of at least two oligonucleotides suitable for ligation together at a third ligation junction and for hybridization without mismatch to a third nucleotide sequence, the third nucleotide sequence being complementary to the first nucleotide sequence and
- 25 present in a second strand of the defective DNA molecule;
- providing a fourth oligonucleotide set of at least two oligonucleotides suitable for ligation together at a fourth ligation junction and for hybridization without mismatch to a fourth nucleotide sequence, the fourth nucleotide sequence being complementary to the second nucleotide sequence and
- 30 present in a second strand of the normal DNA molecule;
- providing a ligase;
- blending the sample, the first set of oligonucleotides, the third set of oligonucleotides, and the ligase to form a first amplification mixture;

blending the sample, the second set of oligonucleotides, the fourth set of oligonucleotides, and the ligase to form a second amplification mixture; and  
subjecting the first and second amplification mixtures to a series of cycles comprising a denaturation treatment, and a thermal hybridization treatment  
5 to amplify exponentially the first, second, third, and fourth sequences, wherein the oligonucleotides of the third oligonucleotide set are complementary to the oligonucleotides of the first oligonucleotide set with an oligonucleotide from the first oligonucleotide set complementing an oligonucleotide from the third oligonucleotide set with a single base overhang and wherein the oligonucleotides  
10 of the fourth oligonucleotide set are complementary to the oligonucleotides of the second oligonucleotide set with an oligonucleotide from the second oligonucleotide set complementing an oligonucleotide from the fourth oligonucleotide set with a single base overhang.

15 4. The method according to claim 3, wherein the ligase is thermostable ligase which does not become irreversibly denatured and lose its catalytic activity when subjected to temperatures ranging from about 50° C. to 105° C.

20 5. A method for detecting a first nucleotide sequence which differs from a second nucleotide sequence comprising:

providing a sample potentially containing the first and second nucleotide sequences;

providing a first oligonucleotide set of at least two  
25 oligonucleotides suitable for ligation together at a first ligation junction and for hybridization without mismatch to the first nucleotide sequence but not to the second nucleotide sequence, wherein the at least two oligonucleotides hybridize on the first nucleotide sequence;

providing a ligase;

30 blending the sample, the first oligonucleotide set, and the ligase to form an amplification mixture;

subjecting the amplification mixture to a series of cycles comprising a denaturation treatment, and a thermal hybridization treatment; and

detecting the presence of the first nucleotide sequence in the sample by detecting the presence of ligated oligonucleotides of the first oligonucleotide set.

- 5                      6.      The method according to claim 5, wherein the ligase is a thermocyclable ligase which does not become irreversibly denatured and lose its catalytic activity when subjected to temperatures ranging from about 50° C. to 105° C.
- 10                     7.      A method for together amplifying and detecting nucleotide sequences complementary to a first nucleotide sequence and a second nucleotide sequence, wherein the first and second nucleotide sequences differ, comprising:
- providing a sample potentially containing the first and second nucleotide sequences;
- 15                     providing a first oligonucleotide set of at least two oligonucleotides suitable for ligation together at a first ligation junction and for hybridization without mismatch to the first nucleotide sequence, but not to the second nucleotide sequence;
- providing a second oligonucleotide set of at least two
- 20 oligonucleotides suitable for ligation together at a second ligation junction and for hybridization without mismatch to the second nucleotide sequence, but not to the first nucleotide sequence;
- providing a ligase;
- blending the sample, the first set of oligonucleotides, and the
- 25 ligase to form a first amplification mixture;
- blending the sample, the second set of oligonucleotides, and the ligase to form a second amplification mixture;
- subjecting the first and second amplification mixtures to a series of cycles comprising a denaturation treatment, and a thermal hybridization to
- 30 amplify linearly nucleotide sequences complementary to the first nucleotide sequence and to the second nucleotide sequence;

detecting the presence of the first nucleotide sequence in the sample by detecting the presence of ligated oligonucleotides of the first oligonucleotide set; and

5        detecting the presence of the second nucleotide sequence in the sample by detecting the presence of ligated oligonucleotides of the second oligonucleotide set.

8.        The method according to claim 7, wherein the ligase is a thermocyclable ligase which does not become irreversibly denatured and lose its  
10        catalytic activity when subjected to temperatures ranging from about 50° C. to 105° C.